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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/577,285	10/10/2006	Barbara Podobnik	33138-US-PCT	2838

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SANDOZ INC
506 CARNEFIE CENTER
PRINCETON, NJ 08540

EXAMINER	
STOICA, ELLY GERALD	

ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
04/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/577,285	PODOBNIK ET AL.	
	Examiner	Art Unit	
	ELLY-GERALD STOICA	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 6-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 6-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

1. In the amendment to the claims submitted 02/11/2008, Applicant cancelled claims 4 and 5, amended claim 1. Claims 1-3 and 6-15 are pending.

Withdrawn Claim Rejections - 35 USC § 102

2. The rejection of claims 1-3, 6-9 and 12-15 under 35 U.S.C. 102(b) over Liu et al. (U. S. Pat. No.: 6,875,432) is withdrawn in view of the amendment to the claims.

Maintained Claim Rejections

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 3, 6, 7, 12 and 13 remain rejected under 35 U.S.C. 102(b) as being anticipated by Goldenberg et al. (U. S. Pat. No: 6,432,449) for the reasons of record.

On page of the remarks Applicants argue that the gel formulated in the Example 5 is not an aqueous formulation and that the pH set forth in Goldenberg et al. falls outside the scope of the present claims. The arguments were carefully considered but not found persuasive because prior to the gellification, the product was aqueous and

having a pH of the buffer (4.5) and also since the gel is a hydrogel, the composition can be construed as an aqueous viscous composition.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. Claims 1-3, 6-9 and 12-15 are rejected and claims 10-11 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al. (U. S. Pat. No.: 6,875,432) in view of Platz et al. (U. S. Pat. No.: 5, 284,656) and in further view of Sumida et al. (U. S. Pat. No.: 6,776,983).

The claims are drawn to a stable pharmaceutical composition of granulocyte-colony stimulating factor (G-CSF), wherein the composition has a pH value in the range from 4.2 to 4.8 and comprises: a therapeutically effective amount of G-CSF, and an acid, wherein the composition is free of a surfactant. The composition also comprises a

polyol and/or a pH buffering system and/or one or more pharmaceutically acceptable excipient(s). The G-CSF is non-glycosylated and the composition is aqueous. The acid in the composition is selected from the group consisting of acetic acid and HCl and the polyol is selected from the group consisting of sorbitol, glycerol, inositol and mannitol. The pH buffering system is acetic acid/acetate. The polyol is sorbitol, present in an amount of 1%-10% or 3%-8%.

Liu et al. teach a stable formulation of reduced viscosity comprising a protein having a lower pH (~4.0 to ~ 5.3). The pH is altered through the addition of a pharmaceutically acceptable acid, base or buffer, and is added in an amount of at least about 10 mM; the acid, base and/or buffers are monovalent and are selected from the group consisting of acetic acid or hydrochloric acid. The pH is any tenth pH value within those enumerated above; example values are pH 4.0, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2 and 5.3. In another particular aspect, the formulation may (but just as an option, hence other embodiments are surfactant free) further comprises a surfactant such as polysorbate (col. 3, lines 17-43). The invention also contemplates a reconstituted formulation that further comprises a lyoprotectant such as a polyol such as trihydric or higher molecular weight sugar alcohols, e.g. glycerin, dextran, erythritol, glycerol, arabitol, xylitol, sorbitol, and mannitol. One of the proteins encompassed by the invention is G-CSF (col. 6, line 41). The formulations of the invention are administered to a mammal in need of treatment with the protein, preferably a human, in accord with known methods, such as intravenous administration as a bolus or by continuous infusion over a period of time (col. 27, lines 18-23). Inherently this means a liquid

formulation and, since the components of the formulation are all water soluble, it will necessarily be aqueous. Liu et al. does not offer a range for the sorbitol in the composition taught in their invention and does not specify the source of the G-CSF used.

Platz et al. teach stable G-CSF formulations that will typically comprise G-CSF dissolved in water and include a buffer and a simple sugar (e.g., for protein stabilization and regulation of osmotic pressure). Examples of buffers which may be used are sodium acetate, citrate and glycine. Examples of sugars which can be utilized are mannitol and sorbitol, usually in amounts ranging from 1% to 10% by weight of the formulation (col. 3, lines 48-61). Recombinant G-CSF, especially E. coli derived, is used in their invention (col. 4, 17-21) and G-CSF produced in E. coli is non-glycosylated.

It would have been obvious for a person of ordinary skill in the art at the time that the invention was made to try the finite number of sorbitol concentration ranges of Platz et al. for the composition of Liu et al., in a attempt to provide an optimal formulation for the G-CSF composition, since persons of ordinary skill in the art have good reason to pursue the known options within their technical grasp. A person of ordinary skill in the art would have had an excellent expectation of success given the teaching of Liu et al., and Platz et al.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208

USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

On page 5 of their Remarks Applicants argue that Liu et al. discloses G-CSF as part of a laundry list of components that may be used as the protein. The arguments were carefully considered but not found persuasive because as such, G-CSF is properly disclosed in a finite list and it would have been obvious to consider G-CSF from a limited list of options.

On page 5 of their Remarks Applicants argue that Platz teaches away from delivery of G-CSF by injection. The arguments were carefully considered but not found persuasive because the teachings of Platz et al. disclose a stable aqueous formulation and the intended use was not material for a comprehensive reading of the references together.

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1-3 and 8-11 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 of copending Application No. 10583157. Although the conflicting claims are not identical, they are not patentably distinct from each other because the G-CSF composition that is claimed in the Application No. 10583157 can be construed as to be the G-CSF composition that has the limitations claimed in the instant Application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Even though Applicant stated in the Remarks on page 8 that: "a proper terminal disclaimer in accordance with 37 CFR 1.321(c) is being filed with this submission" , the Office has not received any Terminal Disclaimer and thus the Double Patenting rejection is maintained.

Conclusion

10. No claims are allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ELLY-GERALD STOICA whose telephone number is (571)272-9941. The examiner can normally be reached on 8:30-17:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic

Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Manjunath N. Rao, /
Supervisory Patent Examiner, Art Unit 1647